AMERICAN
ASSOCIATION
OF BLOOD BANKS

October 10, 2001

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No.97D-0318 — Draft Guidance for Industry: Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products

Dear Docket Officer:

The American Association of Blood Banks (AABB) is the professional society for over 8,000 individuals involved in blood banking and transfusion medicine and represents approximately 2,000 institutional members, including blood collection centers, hospital-based blood banks, and transfusion services as they collect, process, distribute, and transfuse blood and blood components and hematopoietic stem cells. Our members are responsible for virtually all of the blood collected and more than 80 percent of the blood transfused in this country. For over 50 years, the AABB's highest priority has been to maintain and enhance the safety and availability of the nation's blood supply.

The AABB appreciates the opportunity to comment on this "Draft Guidance for Industry, Revised Preventive Measures to Reduce the Possible risk of Transmission of Creutzfeldt-Jakob Diseases (CJD) and Variant Creutzfeldt –Jakob Disease (vCJD) by Blood and Blood Products." We especially appreciate the explicit statements concerning the need to consider both the safety and availability of the blood supply. The proposed phased-in approach should be helpful in attempting to balance these two concerns. The AABB also appreciates the extensive background information discussion of CJD and vCJD as it relates to the FDA's rationale for blood donor deferral. It clearly explains how the FDA has arrived at these decisions.

We support continued monitoring of scientific information on CJD, vCJD, BSE and other TSEs, as well as the availability of blood for patient needs. Policy must continue to be reevaluated and revised as quickly as possible whenever new information is available.

Additional specific comments will be submitted directly from the AABB interorganizational task forces, the Circular of Information for the Use of Blood and Blood Components (Circular), and the Uniform Donor History Questionnaire (UDHQ). The Circular task force has representatives from AABB, America's Blood Centers (ABC), and liaisons from the FDA, and will comment on the labeling provisions of the guidance. The UDHQ task force also includes the American Blood Resources Association (ABRA), the Armed Services Blood Program Office

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(ASBPO), representatives of other disciplines, and liaisons from the Centers for Disease Control and Prevention (CDC0, and will comment on the proposed donor questions.

In addition to the abovementioned comments, the AABB has the following specific comments:

Section IV A 2, Recommended Donor Deferral Criteria, requires "you should indefinitely defer and appropriately counsel donors....." **The AABB requests that "appropriately counsel" should be deleted.** That language does not appear in any of the other described deferrals in Section A. Further, on June 11, 2001 the FDA issued a final rule "General Requirements for Blood, Blood Components, and Blood Derivatives: Donor Notification." This draft guidance appears to add additional requirements not stated in the final rule. Section 630.6(b)(4) of the rule states, "Where appropriate, information about medical follow-up and counseling." While many blood centers do voluntarily provide or refer donors to counseling, "appropriate counseling" should not be a requirement.

The AABB recommends that the language in section V B be revised to read **"You should immediately retrieve and quarantine for subsequent destruction, all in-date blood components, except for Source Plasma *and recovered plasma* under your control (including Whole Blood, blood components, and Source Leukocytes.)**

Section V B discusses retrieval and quarantine for Blood and Blood Components Intended for Transfusion or Further Manufacture from Donors with Five or More Years Residence in Europe. While in-date Source Plasma is exempted from quarantine and subsequent destruction, recovered plasma is not. This appears to contradict earlier statements in the guidance. Section IV C states that, "Consistent with this recommendation, recovered plasma collected prior to deferral from donors with 5 years or more travel or residence in Europe is still considered acceptable for manufacturing of plasma derivatives." In section IV C, the stated reason for permitting Source Plasma donations is "the likely ability of plasma fractionation processes to reduce TSE infectivity, and the uncertain effects of a deferral upon the supply of plasma." Recovered plasma would be subjected to these same plasma fractionation processes and should not be required to be quarantined and destroyed. Further, the stated reasons for deferring further donations for recovered plasma is to prevent inappropriate use of blood and blood components for transfusion. We agree with prohibiting further donations, but any recovered plasma that has already been collected should not be required to be retrieved.

The term Whole Blood Donor should be replaced with a broader definition to clarify that blood and blood components collected by apheresis and intended for transfusion are included. Numerous places in the draft guidance refer to "Whole Blood and Source Plasma Donors." We believe that the term Whole Blood Donor is intended to incorporate not only Whole Blood, but also any blood component that is intended for transfusion purposes. However, not all blood components intended for transfusion are prepared from Whole Blood. We believe that the FDA intends to include components collected by apheresis, such as plateletpheresis, red cells by apheresis, and plasmapheresis if it is intended for transfusion purposes. A different definition is needed to make this clear.

The AABB appreciates the opportunity to comment on this draft guidance. Any questions may be directed to Kay Gregory, Director Regulatory Affairs, at 910-842-2790 or kayg@aabb.org.

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Sincerely,

Karen Shoos Lipton, JD
Chief Executive Officer

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Re: Docket No.97D-0318

Draft Guidance for Industry: Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products

Dear Docket Officer:

The AABB interorganizational Task Force for redesigning the Uniform Donor History Questionnaire (UDHQ) consists of representatives from the American Association of Blood Banks (AABB), America's Blood Centers (ABC), American Blood Resource Association (ABRA), Armed Services Blood Program Office (ASBPO), and liaisons from the Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), and the Canadian Blood Services. The task force also comprises survey design experts, statisticians and an ethicist who is representing the public. The UDHQ task force is engaged in an extensive process to redesign and simplify the donor questions.

The initial step of this project was to evaluate the current questions and suggest new wording. The new wording was tested in focus groups of experienced donors as well as non-donors. Based on that input, additional changes were made. We are currently in the process of further evaluation, utilizing one-on-one cognitive interviews being conducted by the National Center for Health Statistics. The questions have been posted on the AABB Web site to solicit input from the public and members of the organization. Blood collection personnel will also review the questionnaire. Based on expected feedback from all these sources, additional changes are likely to be made. The final product will be submitted to the FDA for approval.

In terms of questionnaire format, the proposed simplified questionnaire will be grouped by time periods of concern. For example, one header may start: "Have you ever.....?" This would be followed by all the questions related to the time period bounded by "ever". Another example of a time period that would be used as a question header is "1980-1996." The question would start: "From 1980-1996, have you...?" This type of format is supported by the survey design specialists on the Task Force, and was proposed at the October 2000 joint FDA/AABB workshop to redesign the donor history questionnaire.

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The Task Force appreciates this opportunity to comment on the draft "Guidance for Industry - Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products." During the past 18 months, we have conducted focus groups to evaluate the current AABB questions approved by the FDA. The Task Force then modified the questions based on focus group feedback. The alternative wording we are *now* proposing for the August 2001 Guidance questions are based almost exclusively on those previously obtained focus group data. When focus group data were not available for specific questions, the survey design specialists on the Task Force provided the requisite expertise for developing new wording. The Task Force will be conducting focus groups to compare the questions in the Guidance with proposed revisions developed by the Task Force. These focus groups sessions will take place during the first 2-3 weeks of October 2001. However, in order to provide input prior to October 28, 2001, we are providing proposed modifications detailed below. We expect that the data from upcoming focus groups will provide additional insight, and we would request that a time allowance be made for final changes based on anticipated focus group responses.

Specific comments appear below:

Section IV B Recommended Questions to Identify Donors at Increased Risk for CJD

Question 1)

FDA proposal: Have you or any of your blood relatives had Creutzfeldt-Jakob Disease or have you ever been told that your family is at increased risk for Creutzfeldt-Jakob Disease?

TF proposal: Have any of your relatives had Creutzfeldt-Jakob Disease?

Rationale: Focus groups indicate that compound questions are not well understood. The crux of the question is family history or risk of CJD, and simplified language will likely elicit that information. Eliminating the part of the question that asks whether the donor has CJD will reduce the number of false positive responses that would ultimately defer the donor unnecessarily. If the donor had *undiagnosed* CJD, they would answer "no" to this question. Further, if the person did have *diagnosed* CJD, they would be extremely unlikely to appear as a prospective donor, and would most certainly be symptomatic and deferred on that basis if they did present to donate.

Question 2)

FDA Proposal: Have you ever received human pituitary-derived growth hormone?

TF proposal: Have you ever received growth hormone from human pituitary glands?

Rationale: TF proposed wording puts the emphasis on growth hormone and then describes the source in language that survey design experts suggest that donors will understand.

Question 3)

FDA proposal: Have you received a dura mater (or brain covering) graft?

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TF: Agrees with wording.

Section IV D Recommended Questions for Identifying Donors at Risk for Exposure to BSE

1. To identify donors with geographic risk of BSE exposure: Phase I

Question 1)

FDA proposal: Have you lived or visited in the United Kingdom (England, Northern Ireland, Scotland, Wales, the Isle of Man, the Channel Islands, Gibraltar, or the Falkland Islands) from 1980 through 1996? If so, have you spent a total time of 3 months or more in the United Kingdom from 1980-1986?

TF proposal: Between 1980 and 1996 did you spend time that adds up to 3 months or more in the United Kingdom (England, Northern Ireland, Scotland, Wales, the Isle of Man, the Channel Islands, Gibraltar, or the Falkland Islands)?

Rationale: This simplification was suggested by focus groups that evaluated the current question. The structure of the proposed question is similar, with the basic change being in the time period – from 6 months to 3 months.

Question 5)

FDA proposal: Have you received a transfusion of blood, platelets, or plasma in the United Kingdom between 1980 and the present?

TF proposal: Since 1980, have you received a transfusion of blood, platelets or plasma in the United Kingdom?

Rationale: This question should be renumbered as Question 2) so that it immediately follows the previous (Question 1) that also asks about the UK. Preliminary information from the NCHS cognitive interviews suggests that it is difficult to recall the definition of UK unless this question directly follows the one in which UK is first defined.

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Question 4)

FDA proposal: Have you visited or lived in France since 1980? If so, have you spent a total time of 5 years or more between 1980 and the present?

TF proposal: Since 1980 have you spent time that adds up to 5 years or more in France?

Rationale: Simplification. The basic structure of this question is similar to question 1 that has been tested with focus groups. In order to keep the travel questions together, this question should be renumbered as Question 3.

Questions 2 and 3)

FDA proposal: As a current or former member of the U.S. military, a civilian military employee, or a dependent, have you been stationed in Belgium, the Netherlands, or Germany, for 6 months or more, between 1980 and 1990?

As a current or former member of the U.S. military, a civilian military employee, or a dependent, have you been stationed in Spain, Portugal, Italy, Turkey, or Greece for 6 months or more, between 1980 and 1996?

TF Proposal: Are you a current or former member of the U.S. military, a civilian military employee, or a dependent?

> If answer is "yes," ask: Between 1980 and 1996 have you been stationed for 6 months or more in a BSE risk country?

Rationale: Simplification. a) The first question serves as a capture question and clearly identifies the intended audience. The second question then identifies the time frame and the geographic area of concern, and does not need to be answered if the answer to the first question is "no." b) This approach will require the screener to provide a list of BSE countries. It will be more efficient to change such a list instead of changing the entire donor history list of questions each time the BSE country list changes. It is also consistent with the FDA approach suggested for Phase II. c) Using only one time frame 1980 – 1996 is consistent with the announced military approach. While it may defer a few donors unnecessarily, it is easier for the donor to understand and provide more accurate information. In addition, we are concerned that someone may have been stationed in one country, but visited or were on temporary assignment in some of the other countries. A single time frame and a single list of countries are much easier to understand.

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2. To identify donors of Whole Blood who have additional geographic risk of BSE exposure: Phase II

FDA proposal: Have you visited or lived in Europe between 1980 and the present? If so, have you spent a total of 5 years or more in BSE risk countries of Europe between 1980 and the present? (Please include time spent in the UK from 1980 through 1996.)

TF proposal: Since 1980 have you spent time that adds up to 5 years or more in BSE risk countries? (includes time spent in the UK)

Rationale: Simplification. Currently, BSE risk countries are primarily in Europe, but this may change.

3. To identify donors who have been injected with bovine insulin

FDA proposal: Have you at any time since 1980 injected bovine (beef) insulin?

TF proposal: Since 1980 have you ever injected bovine (beef) insulin?

Rationale: Simplification based on focus group input. Starting the question with a time frame retains consistency with the approach for other questions.

Section IV B Recommended Questions for Identify Donors at Increased Risk for CJD

This section requires that whole blood donors be asked the three CJD deferral questions at each donation. **We request that potential donors who qualify for an abbreviated questionnaire that has received FDA approval be required to answer only question 1.** Question 2, concerning human pituitary growth hormone, is not necessary because human pituitary growth hormone is no longer available. Once the donor has answered this question "no" on a long questionnaire, the answer will not change. Question 3 will be covered by other general questions on an abbreviated questionnaire such as Have you had any new medical problems, diagnosis, or treatment?"

Section IV D Recommended Questions for Identifying Donors at Risk for Exposure to BSE.

This section requires a face-to-face interview at the time of first use for each donor, or a computerized interactive donor interview program that includes an audio component. **The task force requests reconsideration of this requirement.** The task force is aware that some facilities do not conduct face-to-face interviews with donors, but permit them to read and answer the questions and then follow up on any donor questions or answers that require further information or explanation. We believe that this methodology is acceptable, especially for those individuals who understand written communication more easily than oral communication. This would be true not only for deaf individuals, but for much of the population. If emphasis of these questions is the reason for this requirement, the draft guidance should explain that and permit methods other than face-to-face interviews.

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The UDHQ requests that the FDA consider adopting the task force proposed language. Once again, we thank you for the opportunity to comment. Any questions can be directed to Kay Gregory at kayg@aabb.org or 910-842-2790.

Sincerely,

Joy L. Fridey, MD
Chair, UDHQ Task Force

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Dear Docket Officer:

The American Association of Blood Banks (AABB) task force on the Circular of Information for the Use of Blood and Blood Components is composed of representatives of the blood community, including AABB and America's Blood Centers (ABC). The task force prepared the most recent version of the Circular and is currently drafting the next version. This Circular is used by the entire blood banking community.

The task force appreciates the opportunity to comment on the labeling proposal in Section VII B of the draft "Guidance for Industry Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products." The guidance states that the labeling to address the theoretical risk of transmission of CJD and vCJD for whole blood and blood components intended for transfusion should appear in the Circular under "Side Effects and Hazards." The following language appears in the current Circular (August 2000) under "Notice to All Users". "*WARNING: Because whole blood and blood components are made from human blood, they may carry a risk of transmitting infectious agents, eg viruses, and theoretically the Creutzfeldt-Jakob disease (CJD) agent.*" The task force believes that this language meets the intent of the draft guidance. Because the draft guidance makes a clear distinction between CJD and vCJD, the task force believes that both CJD and vCJD should be mentioned in the warning. We suggest the following wording:

"*WARNING: Because whole blood and blood components are made from human blood, they may carry a risk of transmitting infectious agents, eg viruses, and theoretically the Creutzfeldt-Jakob disease (CJD) agent and variant Creutzfeldt-Jakob disease(vCJD) agent.*"

Since the risk of CJD and vCJD transmission by blood transfusion is considered to be theoretical, the task force believes that it is more appropriate to place the warning in the section titled "Notice to all Users."

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The task force requests that the guidance be changed to use the language in the current Circular as modified above, and to place that language in the section of the Circular titled "Notice to all Users."

Sincerely,

Karen Cipolone, MT(ASCP)SBB, CQA(ASQ)
Chair
AABB Circular of Information Task Force

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